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EXAMINER	
SASAN, ARADHANA	
ART UNIT	**PAPER NUMBER**
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,201	TANIJIRI ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 2/29/08 are acknowledged.

2. Claims 1 and 4-14 are included in the prosecution.

Response to Arguments

Rejection of claims 1 and 4-14 under 35 USC § 103(a)

3. Applicant's arguments with respect to the rejection of claims 1 and 4-14 under 35 USC § 103(a) as being unpatentable over Shinoda et al. (WO 03/009831) in view of Ishibashi et al. (EP 1 125 576 A1) have been fully considered. Applicant states that Shinoda is disqualified as prior art under 35 USC § 103(c) because the current application and Shinoda, at the time the invention of the subject application was made, were owned by Yamanouchi Pharma Co., Ltd. This was found persuasive and the rejection of 11/16/07 is withdrawn.

4. However, rejections based on a newly found prior art reference follow.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "when necessary" on line 3, which renders the claim indefinite.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1 and 4-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fukui et al. (US 4,772,475), as evidenced by Registry citation for tamsulosin, in view of Ishibashi et al. (EP 1 125 576 A1).

The claimed invention is enteric sustained release fine particles of tamsulosin or its salt that can be contained in tablets that disintegrate in the buccal cavity and a method of producing the enteric sustained release fine particles.

Fukui teaches the active ingredient 5-[2-[2-(o-ethoxyphenoxy)ethylamino]propyl]-2-methoxybenzenesulfonamide hydrochloride (Col. 2, lines 35-38), which is tamsulosin hydrochloride (Please see attached Registry citation for tamsulosin). Fukui teaches that by "properly selecting the kind of an enteric coating agent and properly controlling the compounding ratio thereof at the preparation of the granulation product (active substance-containing units), the granulation product having desired dissolving characteristics can be obtained" (Col. 2, lines 58-64). Release controlling agents such as acrylic acid series copolymers,

cellulose derivatives such as ethyl cellulose, hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, Eudragit L 30 D (Rohm Co., trade name; aqueous suspension of a methacrylic acid-ethyl acrylate copolymer), Eudragit E 30 D (aqueous suspension of an ethyl acrylate-methyl methacrylate copolymer), Aquacoat ECD-30 (aqueous suspension of ethyl cellulose) are disclosed (Col. 3, lines 3-18). Enterosoluble polymers including cellulose acetate phthalate, hydroxypropylmethyl cellulose phthalate, a methacrylic acid methyl methacrylate copolymer (Eudragit L, S) are disclosed (Col. 3, lines 58-61). Fukui teaches that "the release of the physiologically active substance can be controlled by selecting the kind of the release controlling agent and/or … an enterosoluble polymer, the release thereof can be also delayed by subjecting the active substance itself to a hydrophobic treatment. The hydrophobic treatment can be performed by microcapsulating the active substance by, for example, spray congealing method using wax, etc." (Col. 4, lines 3-16). After granulation, the active-substance containing units are formed into tablets (Col. 4, lines 46-48). The size of the granulation product is 0.1 to 1.5mm (which is calculated to be 100μm to 1500μm) (Col. 4, lines 44-45).

Fukui does not expressly teach a particle diameter of approximately 5 to 250μm.

Ishibashi teaches a process for producing spherical fine particles containing a drug that is an easily swallowed, controlled release preparation (Abstract). The fine particles are coated with "enteric coating and slow-release coating" (Page 6, lines 3-7). Regarding the coating of the fine particles, Ishibashi teaches coating with "a water-insoluble and water impermeable acrylic resin polymer, … coating with a multilayer film,

… coating with a mixture of enteric coating agent and water-insoluble coating agent, … (Page 6, lines 17-28). Ishibashi also teaches "examples of easily swallowed, controlled release preparations" (Page 6, lines 31-46) and that the "coated drug-containing spherical microparticles can also be used in the production of conventionally used preparations such as … tablets" (Page 6, lines 47-48). The mean particle size is 200μm, and the preferable particle size is 60-150μm (Page 5, lines 49-50). Dissolution tests (according to the Japanese Pharmacopeia) were performed on the coated fine particles at pH 6.8 to test the enteric coating release (Page 8, lines 32-36).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a tablet with tamsulosin by "microcapsulating" it with enterosoluble polymers, as suggested by Fukui, combine it with the controlled release preparation with spherical fine particles containing a drug, as taught by Ishibashi, and produce the instant invention.

One of ordinary skill in the art would do this because Fukui teaches that the release of the active ingredient can be controlled by selecting the kind of release controlling agent. Since enterosoluble polymers are well known in the art for controlling the release of active ingredients, one with ordinary skill in the art would find it obvious to try to combine the enterosoluble polymers and tamsulosin preparation of Fukui with the fine particle preparation taught by Ishibashi.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of enteric sustained release fine particles would have been obvious over the tamsulosin (Col. 2, lines 35-38), microcapsulating the active substance (Col. 4, lines 3-16) and enterosoluble polymers (Col. 3, lines 58-61) as taught by Fukui. The limitation of the particle size would have been obvious over the mean particle size of 200μm, and the particle size range of 60-150μm as taught by Ishibashi (Page 5, lines 49-50). Regarding the dissolution test limitations disclosed in instant claims 1 and 6, Ishibashi teaches testing the dissolution of the preparation. Since the fine particles have been enterically coated, a person with ordinary skill in the art would find it obvious to test a tablet containing the enterically coated particles first at a low pH (1.2) to ensure a low dissolution rate in the gastric milieu and then at a higher pH (6.8) to ensure the release of the drug in the intestinal milieu. A person with ordinary skill in the art would use the protocols of testing outlined in the pharmacopoeia (in the instant case the Japanese Pharmacopoeia was used). Accordingly, a person with ordinary skill in the art would modify the formulation of the tablet and the enterically coated fine particles in order to achieve the desired dissolution profile for the particular drug (in this case tamsulosin hydrochloride) during routine optimization.

Regarding instant claims 4 and 10-12, the limitation of the dissolution and sustained release of tamsulosin controlled by a controlling film or matrix would have

been obvious to one skilled in the art over the multilayer films for controlled release, as taught by Ishibashi (Page 6, lines 17-28).

Regarding instant claim 5, the limitation of a layer of enterosoluble base as the outermost layer would have been obvious over the enterosoluble polymers used to control the release of the active ingredient, as taught by Fukui (Col. 4, lines 3-16). Since the enteric coating has to protect the active ingredient from gastric acid degradation and allow the dissolution in the intestines one with ordinary skill in the art would use the enteric layer as the outermost layer and the water insoluble layer as the inner layer.

Regarding instant claim 6, the limitation of a method of producing enteric sustained-release fine particles for tablets that disintegrate in the buccal cavity would have been obvious over the processes taught by Fukui (Col. 4, lines 3-16 and lines 46-48) and by Ishibashi (Page 6, lines 17-28).

Regarding instant claims 7-9, the limitations of the water insoluble polymer and the enterosoluble polymer would have been obvious over the water insoluble polymers and enterosoluble polymers taught by Fukui (Col. 3, lines 3-18 and lines 58-61) and by Ishibashi (Page 6, lines 17-28).

Regarding instant claim 13, the particle size limitation would have been obvious over the particle size range of 60-150μm as taught by Ishibashi (Page 5, lines 49-50).

Regarding instant claim 14, the limitation of the enteric sustained-release fine particles made into tablets would have been obvious over the tablets taught by Fukui (Col. 4, lines 46-48) and by Ishibashi (Page 6, lines 47-48).

9. Claims 1 and 4-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Platteeuw et al. (US 2003/0147955) in view of Ishibashi et al. (EP 1 125 576 A1).

Platteeuw teaches tablets that contain tamsulosin (Page 1, [0002]). The tamsulosin is used in the form of a powder or fine particles and can be blended with one or more excipients (Page 2, [0015]). The excipients include matrix forming polymers, water-insoluble polymers, celluloses such as ethyl cellulose, hydroxypropyl cellulose and hydroxypropylmethyl cellulose (HPMC), acrylates, methacrylates and copolymers (Page 2, [0017]). The tablet may optionally contain a release controlling agent such as an acrylate/methacrylate polymer/copolymer EUDRAGIT or CARBOPOL (Page 2, [0019]). The tamsulosin may be microencapsulated and tamsulosin microgranules (with a diameter less than 0.1mm (100μm) may be formulated (Page 3, [0020] and Page 4, [0050]). Release controlling agents such as EUDRAGIT RS PO, METHOCEL K4 MP, CARBOPOL 971P NF and KOLLIDON SR are disclosed (Page 3, [0021]). Dissolution of the dosage form in phosphate buffer of pH 6.8 is as follows: 15-35% in 30 minutes, 40-75% in 2 hours, and 70-100% in 5 hours (Page 3, [0029] – [0032]).

Platteeuw does not expressly teach a particle diameter of approximately 5 to 250μm.

The teaching of Ishibashi with respect to spherical fine particles containing a drug is stated above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a tablet with tamsulosin microgranules and enterosoluble polymers, as suggested by Platteeuw, combine it with the controlled

release preparation with spherical fine particles containing a drug, as taught by Ishibashi, and produce the instant invention.

One of ordinary skill in the art would do this because Platteeuw teaches that the release of the active ingredient can be controlled by selecting the kind of release controlling agent. Since enterosoluble polymers are well known in the art for controlling the release of active ingredients, one with ordinary skill in the art would find it obvious to try to combine the enterosoluble polymers and tamsulosin preparation of Platteeuw with the fine particle preparation taught by Ishibashi.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of enteric sustained release fine particles would have been obvious over the tamsulosin (Page 1, [0002]), tamsulosin microgranules (Page 3, [0020] and Page 4, [0050]) and release controlling agents (Page 3, [0021]) as taught by Platteeuw. The limitation of the particle size would have been obvious over the mean particle size of 200μm, and the particle size range of 60-150μm as taught by Ishibashi (Page 5, lines 49-50). Regarding the dissolution test limitations disclosed in instant claims 1 and 6, Ishibashi teaches testing the dissolution of the preparation. Since the fine particles have been enterically coated, a person with ordinary skill in the art would find it obvious to test a tablet containing the enterically

coated particles first at a low pH (1.2) to ensure a low dissolution rate in the gastric milieu and then at a higher pH (6.8) to ensure the release of the drug in the intestinal milieu. A person with ordinary skill in the art would use the protocols of testing outlined in the pharmacopoeia (in the instant case the Japanese Pharmacopoeia was used). Accordingly, a person with ordinary skill in the art would modify the formulation of the tablet and the enterically coated fine particles in order to achieve the desired dissolution profile for the particular drug (in this case tamsulosin hydrochloride) during routine optimization.

Regarding instant claims 4 and 10-12, the limitation of the dissolution and sustained release of tamsulosin controlled by a controlling film or matrix would have been obvious to one skilled in the art over the multilayer films for controlled release, as taught by Ishibashi (Page 6, lines 17-28).

Regarding instant claim 5, the limitation of a layer of enterosoluble base as the outermost layer would have been obvious over the enterosoluble polymers taught by Platteeuw (Page 3, [0021]). Since the enteric coating has to protect the active ingredient from gastric acid degradation and allow the dissolution in the intestines one with ordinary skill in the art would use the enteric layer as the outermost layer and the water insoluble layer as the inner layer.

Regarding instant claim 6, the limitation of a method of producing enteric sustained-release fine particles for tablets that disintegrate in the buccal cavity would have been obvious over the processes taught by Platteeuw (Page 2, [0019]) and by Ishibashi (Page 6, lines 17-28).

Regarding instant claims 7-9, the limitations of the water insoluble polymer and the enterosoluble polymer would have been obvious over the water insoluble polymers and enterosoluble polymers taught by Platteeuw (Page 3, [0021]) and by Ishibashi (Page 6, lines 17-28).

Regarding instant claim 13, the particle size limitation would have been obvious over the particle size range of 60-150μm as taught by Ishibashi (Page 5, lines 49-50).

Regarding instant claim 14, the limitation of the enteric sustained-release fine particles made into tablets would have been obvious over the tablets taught by Platteeuw (Page 1, [0002]) and by Ishibashi (Page 6, lines 47-48).

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615